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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/776,865	HELLERQVIST, CARL G.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5,8-10,15,16,31,33-38,40-42,45,46 and 59-92* is/are pending in the application.

4a) Of the above claim(s) *5,8-10,41,42,45,46,62,63,65-71,79,80 and 82-88* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,15,16,33-38,40,59-61,64,72-78,81 and 89-92* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 February 2001* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The election filed November 29, 2007, is acknowledged and has been entered.

Applicant has elected the species of the inventions of Groups 1 and 11, wherein said composition comprising an amount of one or more immunogenic Group B β-hemolytic Streptococci toxin receptor peptides comprises a peptide comprising the amino acid sequence of amino acids 8-28 of SEQ ID NO: 2.

Because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 1, 4, 5, 8-10, 15, 16, 31, 33-38, 40-42, 45, 46, and 59-92 are pending in the application. Claims 5, 8-10, 41, 42, 45, 46, 62, 63, 65-71, 79, 80, and 82-88 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species of invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on November 29, 2007.

3. Claims 1, 4, 15, 16, 33-38, 40, 59-61, 64, 72-78, 81, and 89-92 are currently under prosecution.

Priority

4. Applicant's claim under 35 U.S.C. §§ 119(e) and/or 120, 121, or 365(c) for benefit of the earlier filing date of Provisional Application No. 60/179,870, filed February 2, 2000, is acknowledged.

However, claims 1, 4, 15, 16, 33-38, 40, 59-61, 64, 72-78, 81, and 89-92 do not properly benefit under §§ 119 and/or 120 by the earlier filing dates of the priority documents claimed, since those claims are rejected under 35 U.S.C. § 112, first paragraph, as lacking adequate written description and a sufficiently enabling disclosure.

To receive benefit of the earlier filing date under §§ 119 and/or 120, the later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994). See M.P.E.P. § 201.11.

Accordingly, the effective filing date of the claims is deemed the filing date of the instant application, namely February 2, 2001.

Grounds of Objection

Claim Objections

5. Claims 59-61, 72-78, and 89-92 are objected to as being specifically directed in the alternative to the subject matter of non-elected species of invention.

Grounds of Rejection

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 31-38, 40, 72-78, 81, 90, and 92 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 31-38, 40, 72-78, 81, 90, and 92 are indefinite because the claims recite the limitation, "wherein the cancer is […]. There is no antecedent basis in the claim to support the recitation of such a limitation; as such, it cannot be ascertained to which cancer the claim refers. Accordingly, the claims fail to delineate the subject matter that is

regarded as the invention with the requisite clarity and particularity to satisfy the requirement set forth under 35 U.S.C. § 112, first paragraph.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1, 4, 15, 16, 31, 33-38, 40, 59-61, 64, 72-78, 81, and 89-92 are rejected under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for making** a composition comprising a peptide consisting of amino acids 8-28 of the amino acid sequence of SEQ ID NO: 2 and a composition comprising a polypeptide comprising of the amino acid sequence of SEQ ID NO: 2, **while being enabling for using** a process for eliciting an immune response in a mammal, said process comprising administering to said mammal any of said compositions, **while being enabling for using** a process for attenuating the progression of the growth in size of melanomas or Lewis lung tumors in mice, said process comprising administering to said mice a composition comprising a peptide consisting of amino acids 8-28 of the amino acid sequence of SEQ ID NO: 2, a peptide consisting of amino acids 112-125 of the amino acid sequence of SEQ ID NO: 2, and a peptide consisting of amino acids 49-63 of the amino acid sequence of SEQ ID NO: 2, **and while being enabling for making and/or using** any subject matter encompassed by the claims, which is taught in the prior art, **does not reasonably provide enablement for making and/or using** the claimed subject matter. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to making and/or using the invention commensurate in scope with these claims.

Beginning at page 10 of the response filed August 14, 2007, Applicant has traversed the propriety of maintaining such a ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

M.P.E.P. § 2164.01 states:

> The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Accordingly, even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors, which have been outlined in the Federal Circuit decision of *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), include, but are not limited to, the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed. See also *Ex parte Forman*, 230 USPQ 546 (BPAI 1986).

Therefore, upon careful consideration of the factors used to determine whether undue experimentation is required, in accordance with the Federal Circuit decision of *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), it has been determined that the amount of guidance, direction, and exemplification disclosed in the specification, as filed, would not be sufficient to have enabled the skilled artisan to use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

(a) Claims 1, 4, 15, 16, 59-61, 64, 89, and 91 are directed to a process for attenuating any of a plurality of different types of cancer in any of a plurality of different mammals. The claims are not limited to processes for attenuating cancer in mice alone, nor are the claims limited to processes for attenuating the growth in size of melanomas and/or Lewis lung tumors.

By Example 1, beginning at page 28, the specification describes exemplary experiments in which C57 mice were immunized with a mixture of three peptide

conjugates comprising fragments of the amino terminus of the polypeptide of SEQ ID NO: 2 ("HP59"), namely the peptides designated "Hab1" (a 15 amino acid peptide consisting of the amino acid sequence of amino acids 49-63 of SEQ ID NO: 2), "Hab2" (a 14 amino acid peptide consisting of the amino acid sequence of amino acids 112-125 of SEQ ID NO: 2) and "Hab3" (a 21 amino acid peptide consisting of the amino acid sequence of amino acids 8-28 of SEQ ID NO: 2), which were conjugated to keyhole limpet hemocyanin (KLH) in complete Freund's adjuvant (CFA). According to the text of Example 1, when a positive antibody titer for anti-peptide antibodies was obtained from all experimental mice, the mice were challenged with mouse melanoma B16 cells or mouse Lewis lung carcinoma cells. The specification discloses, as shown in Table 6, that the melanoma tumors of immunized mice were 45% smaller than those of their control counterparts and the Lewis lung tumors of immunized mice were 38% smaller than those of their control counterparts.

These same experiments are described by Fu et al. (*Clin. Cancer Res.* 2001 Dec; 7: 4182-4194) (of record); see entire document (e.g., page 4192, Figure 6).

Notably, Fu et al. discloses that the fusion peptide comprising Hab1 (i.e., the fusion peptide comprising a 15 amino acid peptide consisting of the amino acid sequence of amino acids 49-63 of SEQ ID NO: 2) linked to KLH did not elicit a strong response; see, e.g., page 4186, column 2; and page 4193, paragraph bridging columns. This suggests that Hab1 may not effectively elicit an immune response in mice, and that any attenuation of the growth of tumors in the mice, which might have occurred as the result of the immune response that was elicited, was probably due to the immunogenicity of one or both of the other fusion peptides (i.e., Hab2 and/or Hab3).

Despite such indications, it cannot be known or predicted whether the fusion peptide comprising Hab3 (a peptide consisting of the amino acid sequence of amino acids 8-28 of SEQ ID NO: 2) conjugated to KLH alone can be used as effectively as the combination administered to the mice in the exemplified experiments; yet the claims are directed to a process comprising administering to a mammal (not necessarily a mouse) a composition comprising only a peptide comprising amino acids 8-28 of SEQ ID NO: 2, and not necessarily a peptide that is conjugated to a carrier protein, such as KLH.

In further contrast to the disclosure of these experiments in mice, the claims are directed to a process for attenuating any of a very large plurality of different types of cancer, *not just mouse melanoma or lung carcinoma*, and, in any mammal, *not just experimental mice*.

Might the results obtained in these experiments be extrapolated to predict the outcome of practicing the same process in humans, for example, or any other mammal to achieve the claimed effect of attenuating any of a plurality of cancers in those animals?

The peptide consisting of amino acids 8-28 of SEQ ID NO: 2 used in the experiments may or may not be immunogenic in humans and other mammals.

If the peptide is immunogenic in humans and other mammals, it may not elicit an immune response that is specifically directed against cancer cells in the animals.

If the peptide is capable of eliciting an immune response in humans and other mammals, the immune response may not be effective or sufficient to achieve the claimed effect of attenuating the growth of cancers in those animals.

Much factual evidence has been placed of record to indicate that such unpredictability would preclude the use of the claimed processes without need of further, elaborate, complicated, undue and unreasonable experimentation.

Applicant has been repeatedly reminded that reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

Again, in deciding *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970), the Court indicated the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. "Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention." *Genentech Inc. v. Novo Nordisk A/S*, 42 USPQ2d 1001, 1005 (CA FC 1997).

Given the state of the art, the level of skill in the art, and the unpredictability of the art, as evidenced by the numerous references cited in support of this rejection, and considering the vast difference in the scope of the claims and scope of the examples set forth in the application, it is submitted that the overly broad scope of the claims would

merely serve as an invitation to one skilled in the art to identify an amount of one or more Group B β-hemolytic *Streptococci* (GBS) toxin receptors or immunogenic fragments thereof that can be administered to any mammal to attenuate the onset, growth and/or progression of any type of cancer in the mammal; yet, defining a substance by its principal biological activity amounts to an alleged conception having no more specificity than that of a wish to know the identity of any material with that biological property. See *Colbert v. Lofdahl*, 21 USPQ2d 1068, 1071 (BPAI 1991).

Notably, among the many references cited to show the state of the art, the level of skill in the art, and the unpredictability of the art, Peterson et al. (of record) teaches numerous agents have show exciting activity in preclinical models and yet have had minimal activity clinically; see, e.g., the abstract. Such disappointments, Peterson et al. discloses, "have led to reasonable skeptism about the true value of both syngeneic and xenograft rodent tumour models in accurately identifying agents that will have important clinical utility" (abstract).

Schuh (of record) reviews the trials, tribulations and trends in tumor modeling in mice to disclose, for example, that "[c]ommon reliance on survival and tumor burden data in a single mouse model often skews expectations towards high remission and cure results; a finding seldom duplicated in clinical trials" (abstract). Furthermore, Schuh discloses, "[d]espite historical significance and ongoing utility, tumor models in mice used for preclinical therapeutic intervention often error towards false positive results and curing cancer in mice" (page 62, column 1).

Kelland (of record) states mouse models are of limited value, because, among other reasons, the mechanisms of action of treatment strategies, such as that disclosed in this application, rely upon the recruitment of the host's (i.e., mouse) immune response, which differs from or is not reflective of that found in man (page 834, column 2). With such limitations of the xenograft model in mind, Kelland suggests that the case for using the model within a target-driven drug development cascade need to be justified on a case-by-case basis (page 835, column 1). Still, Kelland et al. does not altogether discount the usefulness of such models, since, at present, "it is premature and too much a 'leap of faith' to jump directly from *in vitro* activity testing (or even in silico methods) to Phase I

clinical trials (via preclinical regulatory toxicology)" (page 835, column 2). Notably, however, Kelland does not advocate the use of a single xenograft model to exhort one to accept assertions of the effectiveness of treating multiple and different types of cancer in any of a plurality of different mammals, including humans, using the same agent, as has been done in the instant application. Again, Kelland compels one to decide on a case-by-case basis whether such a model is suitable or not; and would not advocate the use of the Lewis lung tumor model, for example, to predict the effectiveness of a treatment modality for other types of cancer.

As recently as August 2006, Dennis (*Nature*. 2006 Aug 7; **442**: 739-741) continues to report, despite their present indispensableness, mouse models, such as xenografts, have only limited utility in predicting the clinical effectiveness of anticancer treatments; see entire document (e.g., page 739, column 2). Dennis explains there is a "laundry list" of problems associated with the use of mice to model human diseases, such as cancer (page 739, column 1). Accordingly, Dennis reports, "[a]lthough virtually every successful cancer drug on the market will have undergone xenograft testing, many more that show positive results in mice have had little or no effect on humans, possibly because the human tumours are growing in a foreign environment" (page 740, column 1). Therefore, quoting Howard Fine, Dennis concludes: " 'Mice are valuable but they are, after all, still mice' ", suggesting the best study subject will always be the human (page 741, column 3).

As previously noted, Saijo et al. (of record) reviewed the reasons for negative phase III trial of molecular-target-based drugs and their combinations; see entire document (e.g., the abstract). Saijo et al. discloses that while numerous phase III trials have been conducted upon the basis of promising preclinical data such as that disclosed in the instant application, few have yielded strongly positive results, and the majority of results have been negative (e.g., abstract). Saijo et al. discloses that there are problems in preclinical prediction of combined effects of anticancer drugs, and the results of preclinical prediction of combined effects have been very poor (page 773, column 2). Saijo et al. teaches many reasons for the poor predictability of combined effects (page 774, Table 6), but Saijo comments such failure may occur because the molecular targets

are not essential for growth, invasion, or metastasis of the tumor (paragraph bridging pages 772 and 773).

Pointedly, there is no factual evidence of record suggesting that HP59, for example, is essential for growth, invasion, or metastasis of any and all types of tumors; and Bodey et al. (*Anticancer Research.* 2000; **20**: 2665-2676) (of record) teaches despite promising, even tantalizing results *in vitro* and *in vivo*, especially with animal models, the failure of cancer vaccines is predicated by very relationship between the tumor and the host immune system, which effectively makes the use of cancer vaccines futile:

> Malignant tumors undergo constant microevolution. Natural selection of the most advantageous surface IP [immunophenotype] involves constant modulation of previous IPs. Progressive dedifferentiation characterizes all neoplastically transformed cells. During this process, numerous 'novel' cell surface antigens appear, are modified and thus do not present the host's immune system with some immunogenic elements. The leukocytic inflammatory infiltrate contains cells with divers capabilities including neutrophils, macrophages and other professional APCs [antigen-presenting cells], as well as T lymphocytes. In situ activation of TAA [tumor-associated antigen] specific CTL [cytotoxic T-lymphocyte] clones occurs and thousands of tumor cells are lysed. However, as we would expect from any population in danger of extinction, the cells of the neoplastically transformed mass proceed with their microevolution and numerous clones of tumor cells survive each repeated attack by the immune system through secretion of immunoinhibitory cytokines, downregulation of MHC molecules, loss of costimulatory molecules, and induction of clonal T cell anergy, among other as yet uncovered ways. This process continues until the 'creation' (ironically as it may sound, by the host's immune system) of highly resistant, poorly immunogenic, and extremely aggressive clones of tumor cells. This is the reality of cancer progression: a back-and-forth struggle between host and tumor, with evolutionary dynamic exchanges throughout the entire process. Use of cancer vaccines to stimulate the immune system may be in vain" (citations omitted) (pages 2673-2674).

The Office's position is further supported by Wang et al. (*Exp. Opin. Biol. Ther.* 2001; **1** (2): 277-290). Wang et al. teaches the "melanoma model" is the paradigm for studies of the effectiveness of T-cell-directed cancer vaccines; see entire document (e.g., the abstract). Wang et al. teaches, "the success of these approaches has been limited [save for scattered reports] and T-cell-directed vaccination against cancer remains at a paradoxical standstill whereby anticancer immunisation can be induced but it is not sufficient, in most cases, to induce tumour regression" (abstract). In order to explain the lack of clinical success, despite the promise of preclinical data, Wang et al. teaches, among other reasons, clinical data suggest the possibility of a dissociation between immune responses detected in peripheral blood *versus* tumor, which suggests that is more

important to determine immune response at the tumor site, rather than in the peripheral blood, in assessing the likely effectiveness of the treatment (page 281, column 1). Regardless of the cause for such poor extrapolation of preclinical findings, Wang et al. discloses the difficulty of correlating laboratory findings with clinical outcome is a significant obstacle to the assessment of the role of immune escape and/or tolerance in cancer progression (page 282, column 2). Furthermore, Wang et al. teaches, "[t]he published experience using the ELISPOT [assay] to monitor T-cell responses to cancer antigens is still limited" (page 283, column 2); and Wang et al. teaches the same is true of the "tetramer" assay (page 284, column 2). Wang et al. teaches, "there are no universally accepted correlates at this time between any method of in vitro immune monitoring and clinical outcome" (page 285, column 1).

Thus, due in part to the inadequacy of the methods used to assess the immune response mustered upon vaccination and the poor correlation of such results and clinically relevant endpoints, such as tumor regression, the art of cancer immunotherapy is highly unpredictable.

Bodey et al. (*supra*) teaches, "while cancer vaccine trials have yielded tantalizing results, active immunotherapy has not yet become an established modality of anticancer therapy" (page 2665, column 2). As to the current state of the art, Bodey et al. comments, "the use of active specific immunotherapy (ASI) for cancer (cancer 'vaccines') is still in its scientific infancy despite several decades of clinical and basic research" (page 2668, column 2). Thus, little has changed to alter the artisans' expectations of the still prospective immunotherapy since the invention was made. Cox et al. (*Science.* 1994; **264**: 716-719) (of record) teaches, "neither adoptive transfer of melanoma-specific CTLs nor specific active immunotherapy with whole melanoma cells or cell-derived preparations has led to the eradication of melanoma in more than a minority of patients" (page 716, column 2). Then again, even that small note of promise has since faded. Bodey et al. discloses, "ASI in at least one instance may have cured melanoma in a patient with metastatic disease, but that patient developed another immunologically and genetically distinct melanoma" (page 2668, column 2). In the abstract Bodey et al. speculates upon the reasons that ASI is ineffective or lacks efficacy:

> The theoretical basis for all of these approaches is very well founded. Animal models, albeit highly artificial, have yielded promising results. Clinical trials in humans, however, have been somewhat disappointing. Although general immune activation directed against the target antigens contained with a cancer vaccine has been documented in most cases, reduction in tumor load has not been frequently observed, and tumor progression and metastasis usually ensue, possibly following a slightly extended period of remission. The failure of cancer vaccines to fulfill their promise is due to the very relationship between host and tumor: through a natural selection process the host leads to the selective enrichment of clones of highly aggressive neoplastically transformed cells, which apparently are so dedifferentiated that they no longer express cancer cell specific molecules. Specific activation of the immune system in such cases only leads to lysis of the remaining cells expressing the particular TAAs [tumor associated antigens] in the context of the particular human leukocyte antigen (HLA) subclass and the necessary costimulatory molecules. The most dangerous clones of tumor cells however lack these features and thus the cancer vaccine is of little use.

The goal of tumor vaccination is the induction of tumor immunity to suppress the growth of tumors. However, Ezzell (*Journal of NIH Research*. 1995; **7**: 46-49) (of record) states that tumor immunologists are reluctant to place bets on which cancer vaccine approach will prove effective in the long run (see the entire document, particularly last paragraph). Ezzell further teaches that no one is very optimistic that a single peptide will trigger an immune response strong enough to eradicate tumors or even to prevent the later growth of micro-metastases among patients whose tumors have been surgically removed or killed by radiation or chemotherapy (page 48, paragraph 6). Published more recently, Bodey et al. (*supra*) states, “there should be caution about assuming that a single epitope or even a few epitopes combined will be as effective ‘crude’ materials, which might better be thought of as ‘polyvalent’” (page 2668, column 2). Spitler (*Cancer Biotherapy*. 1995; **10**: 1-3) (of record) recognizes the lack of predictability of the nature of the art when she states, "ask practicing oncologists what they think about cancer vaccines and you're likely to get the following response: ‘cancer vaccines don't work’. Ask a venture capitalist or the director of product development at a large pharmaceutical company and you're likely to get the same response" (page 1, paragraph 1).

Whatever avenue the artisan takes, in view of the unpredictability in the art, the rarity and lack of uniformity in the successful application, and the numerous and substantial limitations encountered, the threshold of enablement is high. The specification must enable one of skill in the art to make and to use the invention to

achieve the claimed effect without undue or unreasonable experimentation. To have such success, the use of the invention must elicit a melanoma-specific CTL response against the antigen. Boon (*Advances in Cancer Research*. 1992; **58**: 177-210) (of record) teaches that for successful application of active immunization in human patients, we have to stimulate immune defenses of organisms that have often carried a large tumor burden. Establishment of immune tolerance may therefore have already occurred in the patient and in such cases, active specific immunization will be fruitless, since anergic TCL cannot be activated, will not proliferate, and are deficient in effector function. Several lines of evidence suggest that large tumor burdens can tolerize, or at least depress the capability to respond against the tumor (page 206, paragraph 2).

Even more recently, Shafer-Weaver et al. (*Adv. Exp. Med. Biol.* 2007; 601: 357-368) describes the limited success of immunotherapy as in part attributable to such immune tolerance; see entire document (e.g., the abstract).

Notably, Fu et al. (*supra*) discloses that the likely reason that the peptide-KLH conjugate comprising Hab1 (i.e., the peptide comprising the amino acid sequence of amino acids 49-63 of SEQ ID NO: 2) did not effectively elicit an immune response in mice is that of immune tolerance to "self" antigens; see, e.g., page 4193, paragraph bridging columns.

Furthermore, among other mechanisms for the limited success of therapeutic cancer vaccines, Arceci (*Journal of Molecular Medicine*. 1998; **76**: 80-93) (of record) teaches, "it has been hypothesized that tumor cells may escape immune recognition and subsequent killing by failing to satisfy one or more of the […] requirements for T cell antigen recognition and activation. For example, if antigen presentation does not occur because of low or absent expression of MHC or lack of a recognizable tumor antigen, then tumor cells would not be recognized" (page 83, column 2). Areci continues, "on the other hand, if antigen recognition occurs by T cells but tumor cells do not express a costimulatory molecule, then T cells might become anergic to the tumor cells" (page 83, column 2). Notably, Areci teaches, "most solid tumors usually do not express costimulatory molecules" (page 84, column 1); therefore, it is unlikely that the invention can be used to effectively immunize a patient against most cancers.

There is considerable art indicating that cancer vaccines are ineffective, *even if antigen-specific T-lymphocytes can be activated by immunization protocols*. Lee et al. (*Journal of Immunology*. 1999; **163**: 6292-6300) (of record) teaches, "although comparative ex vivo sensitization of pre- and postvaccination PBMC [peripheral blood mononuclear cells, such as B- and T-lymphocytes] has identified reproducible, vaccine-specific systemic T cell responses to immunization, in the majority of cases no regression is seen" (page 6292, column 1). In studies similar to those that are set forth in the examples in the specification, Lee et al. teaches that melanoma antigen epitopes were identified and that these peptide epitopes were capable of inducing highly specific T cell responses against autologous and some HLA-matched tumor cells. Lee et al. discloses, "these studies gave the impression that vaccines induce powerful immunizations comparable to those demonstrable against common pathogens such as the influenza virus to which individuals are repeatedly exposed throughout their lifetime". However, "in most cases, this **vaccine-induced T cell reactivity still does not lead to tumor regression**" (emphasis added) (page 6299, column 1). One of the reasons for the discrepancy, Lee et al. suggests, may be that in vitro methods, which are commonly used to assess immune post-vaccination immune response, such as cell-mediated cytotoxicity assays, tend to "overestimate quantitatively the strength of the immune reaction within the organism" (page 6299, column 1). Lee et al. catalogs a variety of possible explanations for the lack of efficacy, including clonal deletion, exhaustion, or senescence, which are implicated in the development of systemic, epitope-specific immune tolerance, and inadequate immune response attributable to decreased T cell receptor signaling capacity or circulating immune-suppressive cytokines, but conclude that their data suggest that the extent rather than the quality of the response might be more significant limitation of the vaccination protocol (page 6299, column 2). More specifically, Lee et al. reports, "we were surprised at the relatively low numbers of CTL precursors after vaccination even in patients' samples that boasted an exceptional epitope-specific expansion in vitro" (page 6299, column 2). Lee et al. summarizes the results of their study, teaching that "a peptide-based vaccine can effectively generate a quantifiable T cell-specific immune response in the PBMC of cancer patients, though such a response

does not associate with a clinically evident regression of metastatic melanoma" (abstract). While Lee et al. refers specifically to the treatment of melanoma using a different epitope, the teachings are highly germane to the enablement issues relevant in the instant application, because the severe limitations will undoubtedly be shared by any protocol that uses the claimed invention, and there is no exemplification in the specification that would suggest otherwise. In yet another example, Zaks et al. (*Cancer Research*. 1998; **58**: 4902-4908) (of record) teaches that immunization of patients diagnosed with cancer with a peptide epitope derived from the tumor antigen HER-2/neu/ErbB2 leads to activation of peptide-specific cytotoxic T-lymphocytes, but that the T-lymphocytes fail to recognize tumor cells that express the antigen. Zaks et al. discloses their experience is not unique (page 4907, column 2). Gao et al. (*Journal of Immunotherapy*. 2000; **23**: 643-653) (of record) discloses the finding that, although antitumor CTL response was enhanced by immunization, the tumors failed to regress. Gao et al. teaches that the observed lack of regression was associated with a lack of CTL migration to the tumor sites (abstract). Thus, activation of peptide epitope-specific CTL *is not an appropriate endpoint* and a prediction or estimation of efficacy based only upon such data is imprudent or inexact.

Moreover, many attempts to provide efficacious therapeutic immunotherapy for cancer patients have paradoxically failed; despite evidence of that vaccination has induced proliferation of tumor antigen-specific CTL, no major protective antitumor response was seen over and over again in these cases. This subject has been reviewed by Bocchia et al. (*Haematologica*. 2000; **85**; 1172-1206); see entire document (e.g., the abstract).

There are many reasons that the promise of pre-clinical endeavors is broken once clinical trials ensue. Among the possible reasons, with regard to animal models, tumors tend to be highly immunogenic and thus quite unlike most human cancers. Gura (*Science*. 1997; **278**: 1041-1042) (or record) discusses the limitations of animal and cell models. Gura teaches that since formal screening began in 1955, many thousands of drugs have shown activity in either cell or animal models, but that only 39 have actually been shown to be useful for chemotherapy (page 1041, first and second paragraphs).

Sadly, Gura reports that using xenograft animal models to evaluate the potential of novel antitumor therapies often leads to the discovery of " 'good mouse drugs rather than good human drugs' " (page 1041, column 2), because the results acquired using animal models or cell culture are not correlative with those acquired in the clinic. Additionally, with regard to lack of correlation, Lee et al. (*supra*) caution, "it is likely that the immune responses judged after ex vivo expansion of postvaccination PBMC overestimate quantitatively the strength of the immune reaction within the organism" (page 6299, column 1); and Wang et al. (supra) similarly comments upon the inadequacy of assessing immune response by the methods at hand. The magnitude of the immune response that might be sufficient to protect a mammal (e.g., a human) against a tumor is unknown.

Finally, despite any assertion in the specification that the immune response against the mixture of the three particularly described peptide-KLH conjugates is effective to stem tumor neovascularization, Fujiwara (*Vasc. Med.* 2006 May; **11** (2): 115-121), for example, teaches "endothelial cells (ECs), the main component of vasculature, are heterogeneous, as revealed by our phenotypic and molecular biological studies in the laboratory, and it is still hard to adequately understand the molecular mechanisms of angiogenesis and vasculogenesis" (abstract); see entire document. Similarly, Onofri et al. (*J. Endocrinol.* 2006 Oct; **191** (1): 249-261) teaches, in pituitary tumors, a heterogeneous VEGFR expression pattern was observed by immunohistochemistry; see entire document (e.g., the abstract). So, since the vasculature of tumors is *not* homogeneous, and not universally characterized by expression of targeted gene products (e.g., HP59 in humans), the effectiveness of the claimed invention to attenuate the growth of any type of cancer in any mammal is not assured by the example set forth in this application.

It is for all of these reasons that it is submitted that the claimed processes could not be used to achieve the claimed effect without undue and/or unreasonable experimentation.

In addition, inasmuch as the claims are directed to products that are not adequately described in the specification to permit the skilled artisan to immediately envision, recognize, or distinguish those products, or to enable the skilled artisan to make those products without undue and/or unreasonable experimentation, the processes cannot

be used in a manner that would satisfy the enablement requirement. The particular reasons follow.

(b) Claims 1, 4, 15, 16, 31, 33-38, 40, 59-61, 64, 72-78, 81, and 89-92 are directed to a genus of structurally and/or functionally disparate peptide or polypeptides, which as explained in the following rejection are not adequately described in the specification, as filed, to satisfy the written description requirement.

For example, claim 1 is directed to a protein (i.e., a "receptor") having an amino acid sequence of HP59 or SP55 or an amino acid sequence of HP59 or SP55 with at least one conservative amino acid substitution.

At page 9, lines 18 and 19, the specification defines the claim terms, “a” and “an” as referring to a plurality; and a sequence is understood to mean at least any two contiguous amino acids in any given sequence of amino acids.

Accordingly, claim 1, for example, is directed to a protein having at least two contiguous amino acids of the amino acid sequence of HP59 or SP55. Because the specification discloses that HP59 and SP55 comprises the amino acid sequences of SEQ ID NOs: 2 and 4, respectively[1], claim 1 encompasses any protein having at least two contiguous amino acids of the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 4.

It follows that the claims are directed to any of an extraordinarily large genus of structurally disparate peptides or polypeptides.

Although claim 1, for example, recites a limitation requiring the composition comprising this protein be administered in an amount effective to induce or maintain an immune response in the mammal to at least one of the one or more proteins of which the composition is comprised, every peptide or polypeptide is expectedly immunogenic in at least one mammal; and so this functional attribute of the protein or proteins is not specific to their natures and/or structures. Moreover, as explained below, because their structures vary so substantially, it is evident that there is no correlation between any one common structural feature of at least a substantial number of the peptides or polypeptides and any one common functional feature.

[1] See page 9, Table 1, of the specification.

This strongly suggests that the amount of guidance and direction would not be sufficient to enable the skilled artisan to make and then use compositions comprising such structurally and functionally disparate peptides or polypeptides to attenuate the growth of any form of cancer in a mammal, as is the claimed effect of the invention of claim 1, for example.

What has not been adequately described in a manner that would immediately permit the skilled artisan to envision, recognize or distinguish that materials structure cannot be made, certainly not without undue and unreasonable experimentation.

Further addressing the breadth of the subject matter encompassed by claim 1, for example, since any and all amino acids may be "conservatively" substituted by another amino acid in any given sequence, and the claim is specifically directed to a protein having an amino acid sequence of HP59 or SP55 with at least one conservative amino acid substitution, the claim encompasses *virtually every peptide or protein* known or yet to be discovered, which might be formulated as a composition, which when administered to a mammal, is capable of attenuating the growth or advancement of a solid vascularized tumor in the mammal. The peptide or protein need not have any particular structure since it may comprise any amino acid sequence.

Certainly the amount of guidance, direction and exemplification set forth in this application is not reasonably commensurate with claims of such breadth, so as to enable the production and/or use of the claimed subject matter without undue and/or unreasonable experimentation.

Again Applicant is reminded that reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

In conclusion, upon careful consideration of the factors used to determine whether undue experimentation is required, in accordance with the Federal Circuit decision of *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the amount of guidance, direction, and exemplification disclosed in the specification, as filed, is not deemed sufficient to have enabled the skilled artisan to make and/or use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

10. The rejection of claims 1, 4, 15, 16, 31, 33-38, 40, 59-61, 64, 72-78, 81, and 89-92 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is maintained. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Beginning at page 11 of the response filed August 14, 2007, Applicant has traversed the propriety of maintaining such a ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

This is a "written description" rejection.

The considerations that are made in determining whether a claimed invention is supported by an adequate written description are outlined by the published Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, para. 1, ``Written Description'' Requirement (Federal Register; Vol. 66, No. 4, January 5, 2001; hereinafter "Guidelines"). A copy of this publication can be viewed or acquired on the Internet at the following address: <http://www.gpoaccess.gov/>.

These guidelines state that rejection of a claim for lack of written description, where the claim recites the language of an original claim should be rare. Nevertheless, these guidelines further state, "the issue of a lack of written description may arise even for an original claim when an aspect of the claimed invention has not been described with sufficient particularity such that one skilled in the art would recognize that the applicant has possession of the claimed invention" (*Id.* at 1105). The "Guidelines" continue:

> The claimed invention as a whole may not be adequately described if the claims require an essential or critical feature which is not adequately described in the specification and which is not conventional in the art or known to one of ordinary skill in the art. This problem may arise where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process.

With further regard to the proposition that, as *original* claims, the claims themselves provide *in haec verba* support sufficient to satisfy the written description requirement, the Federal Circuit has explained that *in ipsis verbis* support for the claims in the specification does not *per se* establish compliance with the written description requirement:

> Even if a claim is supported by the specification, the language of the specification, to the extent possible, must describe the claimed invention so that one skilled in the art can recognize what is claimed. The appearance of mere indistinct words in a specification or a claim, even an original claim, does not necessarily satisfy that requirement. The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). *See also:* University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 1892 (CA FC 2004).

Thus, an original claim may provide written description for itself, but it must still be an adequate written description, *which establishes that the inventor was in possession of the invention*.

Given the broadest reasonable interpretation that is consistent with the specification and that which would be understood by the artisan of skill in the art, the claims are directed to a genus of structurally and/or functionally disparate polypeptides that comprise an amino acid sequence (i.e., at least two contiguous amino acids of any given sequence) of either HP59 (SEQ ID NO: 2) or SP55 (SEQ ID NO: 4). Moreover, as explained in the above rejection, claim 1, for example, is broadly but reasonably directed to a composition comprising virtually any peptide or polypeptide, which need not have any particular structure or function, provided that it can be administered to a mammal in an amount effective to achieve the claimed effect.

While the specification describes two polypeptides, namely the polypeptides of SEQ ID NO: 2 and SEQ ID NO: 4, the specification fails to describe how these polypeptides are representative of the genus, as a whole, to which the claims are directed. Moreover, the claims fail to recite and the specification fails to describe a particularly identifying (i.e., substantial) structural feature that is shared by the members of the genus of polypeptides to which the claims are directed, which correlates with a particularly

identifying functional feature also common among members of the genus, such that it would be possible to immediately envision, recognize or distinguish at least a substantial number of those members. Therefore, the claims are directed to a genus of polypeptides that vary in substantially in both structure and function; yet, the specification only describes two such polypeptides. As such, the specification would not reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed.

Guidelines states, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). Guidelines further states, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species *cannot* be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. Because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant had possession of the claimed invention at the time the application was filed.

In addition, the description of the few particularly described members of the claimed genus of peptides or polypeptides to which the claims are directed is not sufficient to meet the requirements of 35 USC § 112, first paragraph, since the genus

embraces widely variant members and an adequate description of such cannot be achieved by describing members, which are not representative of the genus. As disclosed and claimed, the genus of molecules does not comprise members having a common, particularly identifying structural feature that correlates with a common functional feature shared by at least a substantial number of its members. As such, absent any of the factual evidence of an actual reduction to practice discussed above, the skilled artisan could not immediately envision, recognize, or distinguish at least a substantial number of the members of the claimed genus said at least substantial number. Accordingly, the specification would not reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed.

The Federal Circuit has decided that a patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. See *Noelle v. Lederman*, 69 USPQ2d 1508 1514 (CA FC 2004) (citing *Enzo Biochem II*, 323 F.3d at 965; *Regents*, 119 F.3d at 1568).

Furthermore, Applicant is reminded that "generalized language may not suffice if it does not convey the detailed identity of an invention." *University of Rochester v. G.D. Searle Co*., 69 USPQ2d 1886 1892 (CAFC 2004). In this instance, there is no language that adequately describes with the requisite particularity the genus of peptides or polypeptides, which can be used to achieve the claimed effect in practicing the claimed invention. A description of what a material does, rather than of what it is, does not suffice to describe the claimed invention.

Furthermore, the Federal Circuit has decided that a generic statement that defines a genus of substances by *only* their functional activity, i.e., the ability to attenuate cancer in a mammal when administered to the mammal, does not provide an adequate written description of the genus. See *The Reagents of the University of California v. Eli Lilly*, 43 USPQ2d 1398 (CAFC 1997). The Court indicated that while applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a precise definition of a representative number of members of the genus, such as by reciting the structure, formula, chemical name, or physical properties of

those members, rather than by merely reciting a wish for, or even a plan for obtaining a genus of molecules having a particular functional property. The recitation of a functional property alone, which must be shared by the members of the genus, is merely descriptive of what the members of genus must be capable of doing, not of the substance and structure of the members.

Although *Lilly* related to claims drawn to genetic material, the statute applies to all types of inventions. "Regardless whether a compound is claimed *per se* or a method is claimed that entails the use of the compound, the inventor cannot lay claim to the subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds, or infringing methods from non-infringing methods". *University of Rochester v. G.D. Searle Co*., 69 USPQ2d 1886 1894 (CAFC 2004). The claimed method depends upon finding the polypeptide having, for example, an amino acid sequence of HP59 or SP55 that may be used in practicing the claimed process to achieve the claimed effect; without such a polypeptide, it is impossible to practice the invention.

Although the skilled artisan could potentially identify peptides or polypeptides that might be used in practicing the claimed invention by screening for candidate polypeptides that are capable of attenuating the growth or progression of cancer in a mammal, it is duly noted that the written description provision of 35 U.S.C § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it.

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*.

Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (CAFC 1991). See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993); *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.,* 18 USPQ2d 1016 (CAFC 1991); *University of Rochester v. G.D. Searle Co*., 69 USPQ2d 1886 1892 (CAFC 2004).

For all these reasons, it is submitted that the subject matter encompassed by the claims is not adequately described in the specification with the requisite clarity and particularity to satisfy the written description requirement, so as to reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. The rejection of claims 31-38, 40, 72-78, 81, 90, and 92 under 35 U.S.C. 102(e), as being anticipated by U.S. Patent No. 6,803,448 B1 (or record), is maintained.

The applied reference has a common assignee and a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Beginning at page 11 of the response filed August 14, 2007, Applicant has traversed the propriety of maintaining such a ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

The rejected claims are directed to a composition comprising a peptide comprising the amino acid sequence of amino acids 8-28 of SEQ ID NO: 2, or of HP59 (i.e., a polypeptide having the amino acid sequence of SEQ ID NO: 2).

U.S. Patent No. 6,803,448 B1 (Hellerqvist et al.) teaches polypeptides that are identical to the polypeptides of SEQ ID NO: 2 and SEQ ID NO: 4; see entire document (e.g., SEQ ID NO: 4 and SEQ ID NO: 8 of the Sequence Listing). Hellerqvist et al. teaches immunogenic fragments of such polypeptides, which are conjugated to KLH (i.e., a "carrier protein"); see, e.g., column 39, Table 8. Hellerqvist et al. teaches making compositions comprising synthetic peptides and Freund's adjuvant, which are injected into rabbits to produce antibodies that bind to the polypeptides; see, e.g., columns 38 and 39, Example 3. Furthermore, Hellerqvist et al. teaches the polypeptides are recombinant polypeptides produced in mammalian host cells; see, e.g., columns 24-26. Hellerqvist et al. teaches the polypeptide are glycoproteins, or proteins that are naturally glycosylated; see, e.g., columns 19 and 20. Because the recombinant polypeptides are expressed in mammalian host cells (e.g., Chinese hamster ovary cells, HeLa cells), the recombinant polypeptides are glycosylated.

Double Patenting

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. The rejection of claims 31, 35, 38, 40, 72, 73, 78, 81, 90, and 92 under the judicially created doctrine of obviousness-type double patenting, as being unpatentable over claims 1-11 of U.S. Patent No. 6,803,448 B1, is maintained.

Beginning at page 12 of the response filed August 14, 2007, Applicant has traversed the propriety of maintaining such a ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

Claims 1-11 of the patent are directed to polypeptides comprising a mammalian GBS toxin receptor or immunogenic fragment thereof, particularly wherein the GBS toxin receptor is identical to the polypeptides of SEQ ID NO: 4 or SEQ ID NO: 8.

SEQ ID NO: 4 and SEQ ID NO: 8 of the patent's Sequence Listing are identical to SEQ ID NO: 4 (SP55) and SEQ ID NO: 2 (HP59), respectively, of the Sequence Listing of the instant application.

The claims of the instant application, on the other hand, are drawn to compositions comprising the polypeptides, or immunogenic fragments thereof, to which the claims of the patent are drawn. Apart from this obvious difference, the claimed inventions are so substantially similar that for the most part, the claimed subject matter of the patent anticipates the claimed subject matter of the instant application; and any other minor differences in the subject matter claimed in the instant application would be seen as an obvious variation of the subject matter claimed in the patent.

With regard to claim 31, for example, of the instant application, it is noted that the claim recites the composition further comprises a "pharmaceutically acceptable carrier" or excipient, which the instant specification defines as including, for example, water soluble formulations that comprise a buffer such as a phosphate buffer, or other organic acid salt, preferably at a pH of between about 7 and 8. It would be obvious to add a buffer to a water-soluble composition comprising the polypeptides to which the patent's claims are drawn.

With regard to claim 35, for example, although the claim recites an intended use for an amount of the claimed composition, the composition itself cannot be materially or structurally distinguished from the obvious composition comprised of the polypeptides or immunogenic fragments thereof to which the patent's claims are directed. The recitation of intended use does not materially or structurally distinguish the claimed subject matter from the obvious variation of the subject matter to which the patent's claims are directed.

With regard to claim 38, for example, which recites the polypeptides of which the claimed compositions are comprised are "recombinant or synthetic", a composition comprising one or more of the polypeptides to which the patent's claims are directed cannot be materially or structurally distinguished from the claimed composition, because although the polypeptides of the claimed composition are "recombinant or synthetic", in this instance and absent a showing otherwise, the process by which the polypeptides are produced is not deemed to impart any material or structurally identifying or distinguishing feature.

With regard to claim 72, for example, which recites a limitation that the peptide is conjugated or linked to a "protein carrier", it is not evident that the "protein carrier" is necessarily a heterologous protein, and might otherwise be deemed the same as the polypeptide of SEQ ID NO: 2, for example, which comprises a peptide comprising the amino acid sequence of amino acids 8-28 of SEQ ID NO: 2 linked to the other amino acids of which said sequence is comprised.

15. Claims 31, 35, 38, 40, 72, 73, 78, 81, 90, and 92 are directed to an invention not patentably distinct from claims 1-11 of commonly assigned U.S. Patent No. 6,803,448

B1. Specifically, although the conflicting claims are not identical, they are not patentably distinct from each other for the reasons set forth above in the obviousness-type double patenting rejection of claims 31, 35, 38, 40, 72, 73, 78, 81, 90, and 92.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned U.S. Patent No. 6,803,448 B1, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 35 U.S.C. 103(c) and 37 CFR 1.78(c) to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

Conclusion

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on (571) 272-0832. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Stephen L. Rawlings/
Stephen L. Rawlings, Ph.D.
Primary Examiner, Art Unit 1643

slr
February 28, 2008